

What is claimed is:

- Sub Q1
1. A particle comprising calcium phosphate, wherein the particle has a diameter between about 300 nm and about 4000 nm, and has a substantially spherical shape and a substantially smooth surface.
 - 5 2. The particle of claim 1, wherein the diameter of the particle is between about 300 nm and about 1000 nm.
 3. The particle of claim 1, further comprising an antigenic material at least partially coating the particle or impregnating the particle or both.
 4. The particle of claim 1, further comprising a natural immunoenhancing factor at least partially coating the particle or impregnating the particle or both.
 - 10 5. The particle of claim 1, further comprising a polynucleotide material at least partially coating the particle or impregnating the particle or both.
 6. The particle of claim 1, further comprising a therapeutic protein or peptide at least partially coating the particle or impregnating the particle or both.
 - 15 7. The particle of claim 1, further comprising a surface modifying agent at least partially coating the particle or impregnating the particle or both.
 8. The particle of claim 7, further comprising at least a partial coating of an antigenic material, wherein the surface modifying agent is at least partially disposed between the surface of the particle and the antigenic material.
 - 20 9. The particle of claim 7, further comprising at least a partial coating of a natural immunoenhancing factor, wherein the surface modifying agent is at least partially disposed between the surface of the particle and the natural immunoenhancing factor.
 10. The particle of claim 7, further comprising at least a partial coating of a polynucleotide material, wherein the surface modifying agent is at least partially disposed between the surface of the particle and the polynucleotide material.
 - 25 11. The particle of claim 7, further comprising at least a partial coating of a therapeutic protein or peptide, wherein the surface modifying agent is at least partially disposed between the surface of the particle and the therapeutic protein or peptide.
- Sub Q2

47. A method for preparing one or more particles of claim 1, comprising reacting a soluble calcium salt with a soluble phosphate salt.

48. The method of claim 47, wherein the soluble calcium salt comprises calcium chloride and the soluble phosphate salt comprises sodium phosphate.

5 49. The method of claim 48, wherein the reacting comprises:

(a) mixing an aqueous solution of calcium chloride with an aqueous solution of sodium citrate to form a mixture,

(b) adding an aqueous solution of sodium phosphate to the mixture to form a solution,

(c) stirring the solution until particles of the desired size and comprising calcium phosphate are obtained.

2 50. The method of claim 49, wherein the concentrations of each of the aqueous calcium chloride, the aqueous sodium citrate, and the aqueous sodium phosphate solutions are independently between about 5 mM and about 100 mM.

15 51. A method for preparing one or more particles of claim 7, wherein the surface modifying agent is at least partially coating the particle, comprising:

(a) adding a surface modifying agent to a suspension of calcium phosphate particles to form a mixture, and

(b) allowing the mixture to stand for sufficient time for the surface modifying agent to cover at least a portion of the particles to form at least partially coated particles.

a 52. The method of claim 51, wherein the surface modifying agent and suspension of calcium phosphate particles are present in a ratio of about 1:20 by volume.

53. The method of claim 51, further comprising contacting the at least partially coated particles with a solution of antigenic material to form particles that are at least partially coated with the antigenic material.

54. The method of claim 51, further comprising contacting the at least partially coated particles with a solution of natural immunoenhancing factor to form particles that are at least partially coated with the natural immunoenhancing factor.

55. The method of claim 51, further comprising contacting the at least partially coated particles with a solution of polynucleotide material to form particles that are at least partially coated with the polynucleotide material.

56. The method of claim 51, further comprising contacting the at least partially coated particles with a solution of therapeutic protein or peptide to form particles that are at least partially coated with the therapeutic protein or peptide.

3 57. The method of claim 49, further comprising adding an antigenic material along with one or more of the aqueous solutions forming the particle, to form one or more particles comprising calcium phosphate that are at least partially co-crystallized with the antigenic material.

58. The method of claim 49, further comprising adding a natural immunoenhancing factor along with one or more of the aqueous solutions forming the particle, to form one or more particles comprising calcium phosphate that are at least partially co-crystallized with the natural immunoenhancing factor.

59. The method of claim 49, further comprising adding a polynucleotide material coding for one or more of the antigens expressed by organisms to be vaccinated against along with one or more of the aqueous solutions forming the particle, to form one or more particles comprising calcium phosphate that are at least partially co-crystallized with the polynucleotide material.

60. The method of claim 59, wherein the polynucleotide material is added in the form of a vector or naked DNA, along with one or more of the aqueous solutions forming the particle, whereby a calcium phosphate biodegradable matrix is formed around the vector or naked DNA, and the vector or naked DNA becomes at least partially embedded in or on the particle.

61. The method of claim 49, further comprising adding a therapeutic protein or peptide along with one or more of the aqueous solutions forming the particle, to form one or more particles comprising calcium phosphate that are at least partially co-crystallized with the therapeutic protein or peptide.

27. The particle of claim 26, wherein the polynucleotide material is selected the group consisting of DNA or RNA sequences encoding one or more epitopes of immunogenic polypeptides presented by virii or cells causing influenza, malaria, colon cancer, hepatitis 3, human immunodeficiency virus, (HIV), simian immunodeficiency virus (SIV), cutaneous T cell lymphoma, herpes simplex, tick born encephalitis, rabies, rotavirus, tuberculosis, Epstein-Barr virus, human papilloma virus, and hepatomavirus.

28. The particle of claim 26, wherein the DNA or RNA sequences are antisense fragments.

29. The particle of claim 26, wherein the polynucleotide material comprises DNA that is inserted into a plasmid vector.

30. The particle of claim 29, wherein the plasmid vector is selected from the group consisting of including pcDNA3 (Invitrogen), pCI (Promega) and PBR231.

31. The particle of claim 29, wherein the plasmid vector expresses cytomegalovirus (CMV) intermediate-early promoter.

32. The particle of claim 29, wherein the plasmid vector expresses bovine growth hormone polyadenylation sequence.

33. The particle of claim 29, wherein the DNA is fused with other DNA sequences in the form of plasmid vector or naked DNA.

34. The particle of claim 33, wherein the other DNA sequences comprise one or more sequences selected from the group consisting of human tissue plasminogen activator leader peptide, bacterial DNA and genes, naked DNA, or portions thereof coding for cytokines or interleukins.

35. The particle of claim 34, wherein the cytokine is granulocyte-macrophage colony-stimulating factor (GM-CSF).

36. The particle of claim 6, wherein the therapeutic protein or peptide comprises a hormone.

37. The particle of claim 36, wherein the hormone comprises insulin.

38. The particle of claim 37, wherein the insulin comprises human insulin.

39. A particle comprising:

5 (a) a core of calcium phosphate, having a diameter between about 300 nm and about 4000 nm, a substantially spherical shape, and a substantially smooth surface,
(b) a surface modifying agent comprising polyethylene glycol at least partially coating the particle, and
(c) human insulin at least partially bonded to the polyethylene glycol,
whereby an effective amount of the particles can be administered in the form of an aerosol to a patient in need thereof.

10 40. A vaccine composition comprising:

- (a) at least one particle of claim 1,
(b) a killed, attenuated, or live vaccine, or a decoy virus, or a particle coated with antigenic material, and
(c) a pharmaceutically acceptable carrier or other excipient.

15 41. The vaccine composition according to claim 40, wherein the at least one particle of claim 1 is combined with a natural immunoenhancing factor and a pharmaceutically acceptable carrier or other excipient.

42. The vaccine composition according to claim 40, wherein the at least one particle of claim 1 is uncoated.

20 43. A vaccine composition comprising:

- (a) at least one particle of claim 3, and
(b) a pharmaceutically acceptable carrier or other excipient.

44. A vaccine composition comprising:

- (a) at least one particle of claim 5, and
(b) a pharmaceutically acceptable carrier or other excipient.

25 45. A pharmaceutical composition comprising:

- (a) at least one particle of claim 6, and
(b) a pharmaceutically acceptable carrier or other excipient.

46. The composition of claim 45, wherein the at least one particle is dried, and wherein the carrier is an aerosol.

62. A method for adjuvanting a vaccine comprising administering an effective amount of at least one particle of claim 1 in conjunction with administration of a killed, attenuated or live vaccine, or a decoy virus to a patient in need thereof.

63. A method for adjuvanting a vaccine comprising administering an effective amount of at least one particle of claim 1 in combination with an effective amount of at least one particle of claim 1 having an antigenic material coating the particle or impregnating the particle or both, to a patient in need thereof.

64. The method of claim 62, wherein the particles are administered in a dosage of about 1 µg to about 1000 µg per kilogram of body weight.

65. A method for providing a controlled release of antigenic material, comprising administering an effective amount of at least one particle of claim 3 to a patient in need thereof.

66. A method for providing a controlled release of natural immunoenhancing factor, comprising administering an effective amount of at least one particle of claim 4 to a patient in need thereof.

67. A method for vaccinating a patient, comprising administering an effective amount of a composition comprising:

- (a) at least one particle of claim 5, and
- (b) a pharmaceutically acceptable carrier solution or other excipient to a patient in need thereof.

68. The method of claim 67, wherein the polynucleotide material is taken up and expressed by cells and translated to produce one or more immunogenic polypeptides that can be recognized by the immune system in a manner similar to the manner in which the polynucleotide material would be recognized if it had been vaccinated conventionally.

69. The method of claim 67, wherein the composition contains about 0.5 to about 500 micrograms of polynucleotide material.

70. The method of claim 69, wherein the composition is administered in a dose from about 0.1 mL to about 2 mL.

71. A method for delivering an inhalable, aerosolizable therapeutic composition comprising administering an effective amount of a composition comprising at least one particle of claim 6 to a patient in need thereof.

72. The method of claim 71, wherein the administering comprises introducing the
5 composition into the patient's lungs.

73. The method of claim 71, wherein the particles are dried.

74. The method of claim 71, wherein the particles are in solution or are combined with a pharmaceutically acceptable carrier or other excipient.

75. The method of claim 71, wherein the particles comprise a coating of polyethylene
10 glycol and human insulin and are administered to a diabetic patient in need thereof.

76. The method of claim 71, wherein the aerosol is administered in a dose from about 50 μ L to about 2 mL.

77. The particle of claim 1, wherein the diameter of the particle is between about 300 nm and about 2000 nm.

15

add
ale